

Setting the stage to quit smoking in Bipolar Disorder patients: brief advice in clinical practice

Preparando el escenario para dejar de fumar en el paciente con Trastorno Bipolar: intervención breve en la práctica clínica

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Abstract

Tobacco consumption is the main preventable factor of mortality in smokers with bipolar disorder (BD), and any possible solutions are often blocked by prejudices over desire, and the possibilities and risks for these patients in giving up tobacco consumption. Adults with BD were recruited at 8 Mental Health Centres. Smokers were evaluated before and after a brief intervention based on the 3 A's and classified into a 'Stage of Change' (SOC) and their 'Readiness to Change' (RTC). A multiple linear regression was used to analyze the progression in their RTC and the independent effect of different variables (pharmacological treatment, history of psychotic symptoms, current anxiety symptoms, willingness, self-perceived capacity to quit smoking and subjective perception of cognitive functioning). Of 212 stable patients diagnosed with BD, current smokers (n=101; 47.6%) were included in the intervention phase, and 80.2% completed it. At baseline, 75.2% were considering the idea of giving up smoking and, after the brief intervention, 30.9% of the patients progressed in their SOC. A significant increase in the level of RTC was observed (53.3 vs 59.3, $P=0.019$). Perception of cognitive performance ($\beta=0.35$; $P=0.002$), the degree of willing to quit ($\beta=0.32$; $P=0.008$), self-perceived capacity to quit tobacco smoking ($\beta=0.30$; $P=0.012$), the patient's age ($\beta=0.72$; $P=0.004$), the age of onset of smoking ($\beta=0.48$; $P=0.022$) and years as a smoker ($\beta=0.48$; $P=0.025$) were all factors that significantly influenced the chances of improving after the short intervention. Smokers with BD consider the idea of quitting and a brief intervention developed in the every day mental health care setting improves the level of readiness. The neurocognitive dysfunction associated with BD may limit patients' readiness to quit smoking.

Keywords: Bipolar disorder; Tobacco; Smoking cessation; Brief advice; readiness to change.

Resumen

El consumo de tabaco es el principal factor prevenible de mortalidad en pacientes con trastorno bipolar (TB), y las posibles soluciones se encuentran bloqueadas por prejuicios acerca del deseo, posibilidades y riesgos al dejar el consumo de tabaco en estos pacientes. En 8 Centros de Salud Mental se reclutaron consecutivamente pacientes con TB. Los fumadores fueron evaluados antes y después de una intervención breve basada en las 3 As y clasificados según los "estadios de cambio" (EC) y su "disposición para el cambio" (DC). Mediante una regresión lineal múltiple se analizó la evolución del DC y su efecto sobre otras variables independientes (tratamiento farmacológico, historias de síntomas psicóticos, presencia de síntomas de ansiedad, deseo de abandono, capacidad auto-percibida y la percepción subjetiva de funcionamiento cognitivo). Se incluyeron 212 pacientes con TB estabilizados, los fumadores activos (n=101; 47.6%) pasaron a la fase de intervención, y un 80.2% la completaron. Basalmente, 75.2% consideraban la idea de dejar de fumar, después de la intervención breve, el 30.9% de los pacientes progresó en su EC. Se observó un incremento significativo del nivel de DC (53.3 vs 59.3, $P=0.019$). La autopercepción del rendimiento cognitivo ($\beta=0.35$; $P=0.002$), el deseo de abandono ($\beta=0.32$; $P=0.008$), la autopercepción de la capacidad para dejar de fumar ($\beta=0.30$; $P=0.012$), la edad del paciente ($\beta=0.72$; $P=0.004$), la edad de inicio del tabaquismo ($\beta=0.48$; $P=0.022$) y los años fumando ($\beta=0.48$; $P=0.025$) fueron los factores que influyeron significativamente en la posibilidad de cambio tras la intervención breve. Los fumadores con TB consideran la idea de dejar de fumar y una intervención breve desarrollada en el marco de la atención a la salud mental diaria, mejoraría el nivel de preparación. La disfunción neurocognitiva asociada con el TB podría limitar la disposición de los pacientes a dejar de fumar.

Palabras clave: Trastorno bipolar; Tabaco; Abandono tabaquismo; Intervención breve; Disposición para el cambio.

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Mental disorders and poverty are currently the niche areas of tobacco consumption in Western populations (Schroeder, 2014). In patients with Serious Mental Illness (SMI), prevalence rates of tobacco use are two to four times higher than in the general population (Diaz et al., 2009). More than half of the patients with bipolar disorder (BD) smoke (Tidey & Miller, 2015; Jackson, Diaz, Lopez & de Leon, 2015) and tobacco is the substance of abuse they consume the most (George, Wu & Weinberger, 2012). They start smoking younger, smoke more intensely – consuming more per day and inhaling more deeply – and have a greater degree of nicotine dependence (Heffner, Strawn, Del-Bello, Strakowski & Anthenelli, 2011).

The mechanisms which may explain this increased prevalence are complex and may involve gene-environmental interaction (Gonzalez-Pinto et al., 1998). The choice of smoking as self-medication, a commonly-debated theory concerning patients with schizophrenia and depressive disorders (Al-Halabi et al., 2017), can apparently be ruled out in BD (de Leon, Diaz, Aguilar, Jurado & Gurpegui, 2006). Compared to BD non-smokers, BD patients who smoke present: more severe symptoms, a higher frequency of rapid cycling, greater risk of suicide, a greater number of hospital admissions (Heffner et al., 2011), a worse quality of life at a mental level (Gutiérrez-Rojas et al., 2008) and a cardiovascular and respiratory mortality rate which is double and triple, respectively, that of the general population (García-Portilla et al., 2010).

Tobacco use is the main preventable risk factor of mortality in this population (Callaghan et al., 2014), and with the increasing evidence of effective and safe of pharmacological and psychological treatments (Anthenelli et al., 2016; García-Portilla et al., 2016; Almadana et al., 2017), the literature stresses the need to address this problem in everyday psychiatric care (Prochaska et al., 2011).

Evaluating the subjects' willingness to change and taking steps to raise motivation and control the factors which limit it, are the first steps in any treatment plan for quitting. In BD, the first trials in smokers have begun recently (Weinberger, Krishnan-Sarin, Mazure & McKee, 2008; Wu et al., 2012; Chengappa et al., 2014; Evins, Cather & Laffer, 2015; Anthenelli et al., 2016; García-Portilla et al., 2016). These trials include patients who have expressed the desire to quit smoking but do not evaluate the initial motivation level specifically. So far, the main references have been from studies in patients with schizophrenia (Etter & Etter, 2004). Weinberger et al. (2008) and Wu et al. (2012) were the first to report serious problems of recruitment since they could not find bipolar patients prepared to attempt to give up. Recently, however, members of our group have published results of a multi-component treatment in a clinical setting (García Portilla et al., 2016), which puts the main emphasis on the preparation and motivation stage, before active treatment is started for schizophrenia and

BD. (Prochaska et al. (2011)) An online survey in the USA revealed that of smokers with BD who had made an average of 4 previous attempts, up to 74% express willingness to quit smoking and only one third had been given a recommendation by their psychiatrist (Prochaska et al., 2011).

Although there are multiple theories to explain the concept of motivation and changes in behaviour (Miller, 2011), the Transtheoretical Model (TTM) developed by Prochaska and DiClemente (1983) has been the reference model for addictions. The TTM algorithm in the Stages of Change (SOC) and the Contemplation Ladder, (Biener & Abrams, 1991) have been the most commonly used scales, in the few studies that have analyzed motivation levels for quitting smoking in people with mental disorders (Siru, Hulse & Tait, 20094). The TTM has been the most widely used tool in research into smoking cessation and recognizes the SOC as starting, transit or arrival points in the process, to which a predictive value of the possibilities of change can be added (Chou et al., 2015). Despite the popularity of the TTM, the debate remains open about whether to use the SOC classification, based on arbitrary cut-off points, or to calculate a 'Readiness to Change' index (RTC) (Ceccarini, Borrello, Pietrobissa, Manzoni & Castelnuovo, 2015).

Success in giving up smoking is proportional to the intensity of the intervention (Fiore & Panel, 2008), but in the first objective of generating motivation, the brief interventions using the 5 A's (Ask, Advice, Assess, Assist and Arrange) and the 3 A's (Ask, Advice and Assess) have been shown to be cost-effective in the general population (Rice & Stead, 2008) and have been endorsed by clinical practice guidelines (West, McNeill & Raw, 2000). The EPA (European Psychiatry Association) guidance on smoking cessation strategies (Rüther et al., 2014) recommends trying out these interventions in smokers with mental illness. In SMI patients, so far only DiClemente et al. (2011) have evaluated the intervention with 5 A's, and point out the importance of the number of repetitions of the first three A's in the long-term possibilities of success in SOC (DiClemente et al., 2011). In BD patients, although the possibilities of the brief intervention are not known, perhaps the first objective of the 3 A's intervention would be to try to increase the smoker's level of readiness through the different stages of motivation for change (pre-contemplation, contemplation, and preparation).

On the other hand, BD is associated with persistent neurocognitive deficits across the broad domains of sustained attention, verbal memory and prefrontal/executive cognition, which in turn are major predictors of patients' functional outcomes (Vieta et al., 2013). Moreover, neuropsychological status is related to decision making and attitudes such as motivation for lifestyle changes: neurocognitive dysfunction may therefore decrease the chances of progress on a motivation level (Baune & Malhi, 2015). In the same way, the anxiety symptoms present in over 50% of patients with BD (Goes, 2015), among other factors which

increase comorbid addictions (Cazard & Ferreri, 2013), worsen the prognosis, require specific treatment and could influence the possibilities of this type of intervention.

The community care environment available to this population offers advantages through the frequency of contacts, the credibility of the health professionals and the regular advice given. Despite these advantages, we are faced with a serious health problem and cost-effective interventions such as the brief 3 A's intervention could serve to identify the level of motivation and raise initial willingness to quit among smokers with BD.

Aims of the study

(1) to describe and quantify the prevalence of smoking and how it is currently dealt within a representative sample of Bipolar Disorder patients studied in a community environment; (2) to learn the level of motivation of smoking bipolar patients, based on Transtheoretical Model; (3) to evaluate the effectiveness of the brief intervention that Asks, Advises and Assesses (3 A's) to raise the patient's motivation level; and (4) to identify the socio-demographic, clinical or smoking variables that may influence the chances the intervention has of success.

Methods

Design and settings

The multi-centre study was conducted according to a mixed design including: (1) a cross-sectional, observational and descriptive study performed at the baseline visit and (2) a post-intervention design, in which patients who were identified as smokers at the baseline visit were given a brief anti-smoking intervention over three sessions.

The study lasted 6 months and was carried out in 8 Mental Health Centres of 4 provinces of Andalusia, in southern Spain (Cordoba, Granada, Jaen and Malaga). The study was given the approval of the Research Ethics Committee of the Reina Sofia University Hospital in Cordoba.

Subjects

Recruitment according to ICD-10 criteria (1992) was carried out consecutively-when attending their scheduled review appointments-among adult patients with BD (18-65 years old) who were clinically stable and attended their scheduled review appointments. Clinical stability and the absence of suicidal behaviour in the 6 months before commencing the study were assessed by the patient's usual psychiatrist. All of them signed to give their informed consent for their data to be used in the study database.

In addition, the patients who were current smokers (1 cigarette or more a day) at the recruitment appointment were invited to participate in the pre- and post-intervention evaluation (Figure 1).

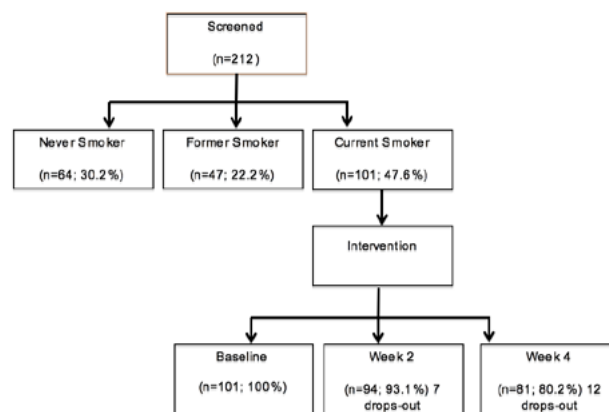


Fig. 1. Recruitment of the subjects and disposition after intervention.

Measurements and outcomes

The total sample was subdivided into 3 groups according to their smoking habits (current smoker, former smoker and never-smoker). Socio-demographic and clinical data were collected from all of them.

Current smokers were assessed using the following instruments at the baseline visit:

The Hamilton Anxiety Scale (HARS) (Hamilton, 1959) was used to assess whether the patient suffered from anxiety symptoms. This scale is hetero-administered by a clinician after an interview in which 0 to 4 points are scored for each item, which assess both intensity and frequency of anxiety symptoms. There are no cut-off points, and a higher score indicates a greater intensity of anxiety.

Fagerström's Nicotine Dependence Test (FTND) (Fagerström, 1978) the modified version of this scale (Heather-ton, Kozlowski, Frecjer & Fagerström, 1991), is hetero-administered and consists of 6 items which evaluate nicotine dependence. The scores are divided into: below 4 (low dependence), 4 - 7 (moderate dependence) and over 7 (high dependence) on nicotine.

The Visual Analogic Scale (VAS) from 0 to 10 was used to measure patients' perceived desire and self-perceived capacity to quit smoking, because its predictive value equivalent to scales with multiple items (Gwaltney, Metrik, Kahler & Shiffman, 2009).

The URICA (University of Rhode Island Change Assessment) (Di Clemente et al., 1991) is a 32-item self-report scale that includes 4 subcategories measuring the stage of change (SOC) based on Prochaska's TTM. Items are rated on a 5-point Likert scale ranging from 1 (strong disagreement) to 5 (strong agreement). The Spanish version of the scale (Gómez-Peña et al., 2011) has shown adequate internal consistency both globally and in each of the 4 sub-scales (between 0.69 and 0.89). Two possible means of evaluation have been described: a) discrete measurements where the highest score ranks the patient on a particular SOC and b) a continuum in which the subscales are combined arithme-

tically (Contemplation + Action + Maintenance - Precontemplation) to produce a second order continuous score which can be used to assess Readiness to Change (RTC). Subjects completed the URICA as a way of carrying out the third A (Assess) at baseline (URICA 1) and week 4 (URICA 2), thus giving us two continuous measurements for RTC. The difference between the two was the main variable for the analysis (RTC_{2-1}).

The COBRA, *disfunción cognitiva en el trastorno bipolar* (Rosa et al., 2013), is a 16-item questionnaire that measures BD patients' perception of cognitive deficits in several areas, such as: executive functions, processing speed, working memory, learning and verbal memory and attention/concentration. Responses are given on a 3-point Likert scale ranging from 0 (never limited) to 3 (always limited). The total score is a result of the sum of the items. We have used the Spanish version, with a Cronbach's alpha of 0.913.

Intervention

A brief motivational intervention to quit smoking was carried out based on the idea of the 3A's (Ask -Do you smoke?, Advice -Advise the patient to quit in a clear, firm and personalized way, Assess -Would you be willing to quit smoking next month?) discussed above (Rice & Stead, 2008), distributed over 3 sessions (baseline, week 2 and week 4) lasting no more than 10 minutes each and with a total duration of 30 minutes. The first and last contacts were conducted face-to-face and the contact at week 2 by phone. At baseline and at week 4, the 3A's were completed, using URICA to measure the readiness to quit, while the phone interview was used to reinforce the advice given in the baseline intervention. To minimize any inter-observer differences, the three interventions were carried out by the same professional (psychiatrist or nurse) in each centre.

Statistical Analyses

Statistical analysis was performed using the SPSS program (version 15.0). Dimensional variables and frequencies were compared by parametric or non-parametric tests, as appropriate. Continuous variables were analyzed by analysis of variance (ANOVA) or Student *t* tests, and categorical variables by chi-square or Fisher's exact tests. Relationships between variables were expressed as Pearson's product-moment (*r*) or Spearman rank-order (*r_s*) correlations. Multiple linear regression, using the conditional back procedure, was used to analyse the independent effect of each variable (pharmacological treatment, history of psychotic symptoms, current anxiety symptoms, willingness, self-perceived capacity to quit smoking and subjective perception of cognitive functioning), and the change of RTC after the intervention. For this reason we calculate a new variable (RTC after the intervention minus RTC before: RTC_{2-1}), the fundamental dependent variable. The multivariate models include the statistically significant variables in the bivariate

analysis or those of special clinical relevance. The statistical significance level was set at $P < 0.05$.

Results

Of 212 patients diagnosed with BD, 101 (47.6%) were current smokers and were included in the intervention phase. Of the remaining patients, 47 were former-smokers and 64 had never smoked. Table 1 shows the socio-demographic, and clinical data of the three groups (smokers, former smokers and never-smokers). On comparing these three groups, we found some differences: the intervention group (current smokers) contained a higher proportion of male patients, patients whose marital status either separated or divorced, unemployed and disabled patients and patients with a comorbid psychiatric disorder. We found no differences as regards level of education, length of illness, presence of psychotic symptoms or pharmacological treatment received (Table 1).

Eighty one patients (80.2%) from the intervention group completed the follow-up. All non-completer cases were due to subjects expressing their wish to abandon the study. We found no statistically significant differences between those who had completed the intervention and those who did not, in the variables analyzed (socio-demographic, clinical and smoking history, SOC, RTC, dependence and anxiety level, self-perception capacity to quit and cognitive function).

In those patients who were current smokers, 80.2% of them had never been offered a specific anti-smoking treatment during the years of follow-up at their mental health centre and 62.1% had never been asked about their smoking habits. In the 'former smokers' group, 75% reported that they had given up smoking without specific treatment and 81.8% reported no clinical worsening of their illness in any way after giving up smoking (this measures were patients self-reported).

In the intervention group, the mean age at onset of smoking behaviour was 18.9 years (SD 7.1), with a mean consumption of around 18.1 cigarettes per day (SD 11.2) for 28.5 years (SD 10.5). 16.8% of these smokers had high nicotine dependence (FTND > 7). 80.2% of the current smokers had tried to quit smoking with an average of 2.7 attempts (SD 2.5), and had achieved an average of 11.8 months without smoking (SD 21.4). The clinical and tobacco use variables are summarized in Table 2.

In the VAS, smokers obtained a score of 6.2 in their willingness to quit smoking (SD 3.4), and 4.7 on their self-perceived capacity of quitting (SD 3.1). In the URICA scale evaluation of level of motivation performed in the first contact (URICA 1), 17 (16.8%) of our patients were in the pre-contemplative phase, 76 (75.2%) in the contemplative phase and 8 (7.9%) in the action stage. 30 days after completing the brief intervention (URICA 2), 30.9% of

Table 1. *Description of the sample*

	Current Smoker (101; 47.6%)	Former Smoker (47; 22.2%)	Never smoker (64; 30.2%)	Statistical test, <i>p</i>
Mean Age (sd)	47.5 (9.8)	49.7(8.2)	50.7(11.1)	2.159 ¹ . 0.118
Gender [n (%)]				
Male	45(56.2)	21(26.2)	14(17.5)	10.056 ² . 0.007
Female	56(42.7)	25(19.1)	50(38.2)	
Marital status [n (%)]				
Never married	28(54.9)	8(15.7)	15(29.4)	11.295 ² . 0.023
Married or cohabiting	35(36.5)	25(26.0)	36(37.5)	
Widowed or separated/divorced	36(61.0)	12(20.3)	11(18.6)	
Educational level [n (%)]				
Without formal studies	8(42.1)	2(10.5)	9(47.4)	6.753 ² . 0.344
Primary school	41(47.1)	17(19.5)	29(33.3)	
Secondary school	33(51.6)	15(23.4)	16(25.0)	
University	18(43.9)	13(31.7)	10(24.4)	
Work status [n (%)]				
Unemployed	22(51.2)	10(23.3)	11(25.6)	16.074 ² . 0.013
Working (full/part-time)	24(55.8)	9(20.9)	10(23.3)	
Disabled (temporary/permanent)	46(51.7)	21(23.6)	22(24.7)	
Others*	9(24.3)	7(18.9)	21(56.8)	
Diagnosis [n (%)]				
Bipolar disorder I	62(45.3)	26(19.0)	49(35.8)	6.087 ² . 0.048
Bipolar disorder II	38(51.4)	21(28.4)	15(20.3)	
Comorbid disorder [n (%)]				
Anxiety disorder	16(55.2)	2(6.9)	11(37.9)	13.996 ² . 0.030
Personality disorder	14(60.9)	2(8.7)	7(30.4)	
Substance use disorder	8(72.7)	3(27.3)	0(0)	
Length of illness, months [Median (range)]	162(536)	168(416)	170(468)	0.731 ¹ . 0.483
Psychotic symptoms, yes [n (%)]	68 (50.4)	31(23.0)	36(26.7)	2.000 ² . 0.368
Treatment, yes [n (%)]				
Mood stabilizers	88(48.9)	37(20.6)	55(30.6)	2.224 ² . 0.329
Antipsychotics	75(47.8)	35(22.3)	47(29.9)	0.050 ² . 0.975
Antidepressants	37(46.2)	16(20.0)	27(33.8)	0.950 ² . 0.622
Benzodiazepines	53(47.3)	21(18.8)	38(33.9)	2.653 ² . 0.265
Hypnotics	19(51.4)	7(18.9)	11(29.7)	0.381 ² . 0.827

Note. *Other includes housewife, student and retired.

1. ANOVA test, 2. Chi-square test.

Table 2. *Current smokers, baseline clinical and smoking characteristics (n=81)*

	Media	(SD)
HAM-A	13.6	10.4
COBRA	13.0	9.5
Self-reported CPD	18.1	11.2
FTND	4.9	2.6
Willingness to quit tobacco smoking	6.2	3.4
Self-perceived capacity to quit tobacco smoking	4.7	3.1
RTC 1	53.3	25.9
RTC 2	59.3	25.9
RTC2-1	7.1	22.5
Number of attempts	2.7	2.5
Mean duration of attempts in months	11.9	21.4

Note. SD: Standard deviation; COBRA: Cognitive complaints in bipolar disorder rating assessment; FTND: Fagerström Test for Nicotine Dependence HAM-A: Hamilton anxiety rating scale. CPD: Cigarettes per day.

Table 3. *Multiple linear regressions of factors associated with change in Readiness to change after the intervention (RTC2-1) in current smokers (n=81)*

Variables	Coefficient of partial correlation (β)		valor <i>P</i>
	t_{exp}		
Readiness to change*			
Age (years)	- 0.72	- 2.96	0.004
Length of smoking (years)	0.58	2.28	0.025
Age at onset of smoking behaviour (years)	0.48	2.34	0.022
Willingness to quit tobacco smoking	0.32	2.71	0.008
Self-perceived capacity to quit tobacco smoking	- 0.30	- 2.57	0.012
COBRA cognition scale score	-0.35	-3.28	0.002

Note. *Coefficient of determination (adjusted R²) = 0.16, F = 3.38, df = 1, 74, P = 0.003.

patients had advanced in their SOC; 7 (8.6%) were in the pre-contemplative phase, 53 (65.4%) in the contemplative phase and 21 (25.9%) in the action stage (Figure 2). Baseline SOC assessed by the 'Readiness to Change' (RTC) continuous quantitative variable showed a significant increase from 53.3 at the beginning, to 59.3 after completing the intervention ($P = 0.019$).

A multiple linear regression model with the number of years that the patient had been smoking, the age at onset of smoking behaviour and the willingness to quit smoking all linked with a greater evolution of the RTC. Moreover, using the total score of the COBRA scale, the variables that were associated with a lower progress on the RTC were age, self-perceived capacity for quitting smoking and subjective cognitive status (Table 3).

Discussion

Concurring with previous results in BD (Diaz et al., 2009; Tidey & Miller, 2015), we found smoking rates that doubled those published in the general population and the recurrent alerts in the literature about the passivity of the patient's normal health care environment have been confirmed (Evins et al., 2015).

Within the conceptual framework of stages of motivation and change process, and for the first time in BD, this study of an anti-smoking intervention conducted in a community setting shows that a low-intensity intervention based on the 3A's has a significant impact on the level of motivation for change in patient who smoke - independently of the degree of tobacco consumption. The subjective perception of the neurocognitive functioning predicted the chances of progress after the intervention.

The 30.9% of the smokers increased their SOC and there was a significant increase in the RTC index - both measurements are based on the Transtheoretical Model of Behaviour Change (Prochaska & DiClemente, 1983). This type of intervention, strongly supported in the literature for generating motivation and attempts to quit smoking in ge-

neral populations (Rice & Stead, 2008), has been scarcely studied in SMI patients who smoke and to date, there is no specific works referring to BD. Di Clemente et al. (2011) reported how up to 60% of patients with psychotic disorders make progress in their SOC when followed up over a year, with a scheduled intervention using the 5 A's. In addition, patients exposed to more frequent repetition of the first 3 A's were the ones that progressed most at this stage.

The level of willingness to quit smoking expressed at the beginning of the intervention, having started smoking later in life and having smoked for more years were the variables that independently predicted a greater advance in readiness to give up after the intervention. These variables also predict the possibilities of a first attempt to give up in the general population (West et al., 2015). It showed that the younger the patient at the time of the intervention, the greater the evolution in the level of readiness. This, in theory, goes against what is usually published in the health advice given to the general population, where older people tend to be more receptive to these kind of interventions (Zolnieriek & Dimatteo, 2009; Marín, Gil & Romero, 2017), but does concur with the favourable characteristics of a recently-published study on first attempt in smokers (Sharma & Szatkowski, 2014). Despite the fact that the psychiatric population has been less receptive to the campaigns to reduce smoking than the general population, those who are younger - who may feel less stigmatized and have failed on fewer occasions - may in fact benefit from them more and be more receptive to the kind of intervention mentioned above. Those smokers who expressed a higher level of self-capacity for change at the start of the intervention improved their level of readiness less. While recognizing the value of self-perceived capacity as a predictor of attempting to give up (Borland et al., 2010), we may assume that in a sample of BD where many of the patients are asked for the first time about their tobacco use and wishes, the self-capacity expressed may have an unrealistic value and offer little insight into the true depth of their problem. This is similar to the conclusion reached in the meta-analysis of smokers from the general population (Gwaltney et al., 2009), where self-capacity was evaluated prior to the attempt to quit.

A greater perception of functional limitation at the neurocognitive level meant that less progress could be made on the level of readiness. Regarding cognition, the present findings are difficult to interpret, since no previous study has examined the potential role of neurocognitive status to predict either changes in motivation or quitting smoking. Some indirect evidence, however, may be extrapolated from studies of smokers with schizophrenia or without psychiatric disorders. In a set of placebo-controlled clinical trials, baseline dysfunction, as measured by sustained attention, spatial working memory and executive cognition, has been associated with the failure of smoking cessation treatment in smokers with schizophrenia seeking treatment

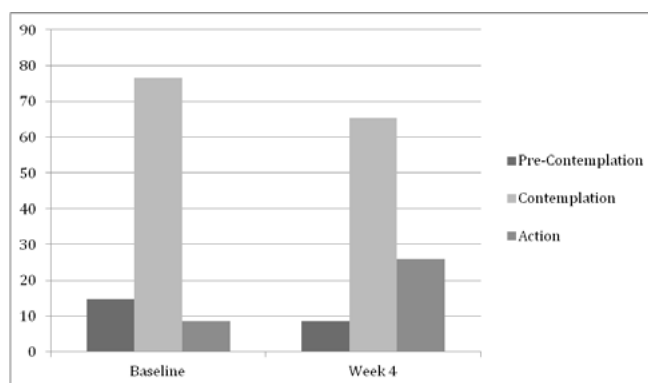


Fig. 2. Motivational stages (before and after the intervention) measured by URICA scale in the intervention group (%).

(Moss et al., 2009). It is worth noting that schizophrenia and BD share a core neurocognitive dysfunction, with high rates of comorbid nicotine dependence and low rates of smoking abstinence. In other clinical populations, cognitive impairments decreased response to treatment among subjects with marijuana or cocaine dependence (Aharonovich, Brooks, Nunes & Hasin, 2008). Moreover, the key cognitive predictors of attaining abstinence in smokers without psychiatric disorders are also sustained attention, working memory and executive functioning (Ashare, Falcone & Lerman, 2014). Since the prefrontal cortex is involved in all these cognitive deficits, it represents a potential target for the development of pharmacological and psychological therapies aimed at treating cognitive deficits. In turn, targeting prefrontal-related dysfunctions may enhance the success rates for giving up smoking in all these populations and possibly also in BD.

In our study, the impact generated was independent of gender, the number of cigarettes per day and the dependency level. In the results found by DiClemente et al (2011), women progressed less than men over one year, and this result was also independent of tobacco consumption and dependence. The literature leaves no room for doubt about the prognostic value of the dependence level on the rates of initial cessation and possible recurrences (Japuntich et al., 2011). Even so, the results we obtained from a BD sample seem coherent with an intervention designed to be carried out in large target populations, with the aim of generating a first approach to the motivation level without specifying the gender or the severity of the smoking addiction (Kruger, O'Halloran, Rosenthal, Babb & Fiore, 2016).

The results of the URICA scale, which positions the patient in a SOC or quantifies an RTC value and its evolution, have a predictive value regarding the possibilities of a treatment designed to break the habit (Chou et al., 2015). Moreover, this is the first study to specifically assess SOC in bipolar smokers. Our results confirm that up to two-thirds of the patients asked about their habit in a normal psychiatric care setting are placed in the contemplation stage, which means that they plan to quit in the next 6 months and therefore could be target patients for intensive treatments. These results are higher than those described in samples of patients with schizophrenia (DiClemente et al., 2011) and, as noted in the age factor, they certainly give us an insight into the greater permeability in BD for changes in tobacco consumption that have occurred in recent years in the general population.

The motivation to change when suffering an addiction plays a key role in recognizing the problem and finding solutions. Although it is urgent to know the level of motivation in this population of smokers and generate steps to increase it, how to quantify the level of motivation and its progress over time remains as a challenge. The concepts of SOC and RTC and their quantification through the URICA

scale constitute a key option in addiction research, but it also has its drawbacks (DiClemente, Schlundt & Gemmell, 2004). Understanding motivation from the SOC allows us to position the patient and provides a model by which we can observe the process of change; however, quantifying it in discrete stages or as a continuum also generates debate (DiClemente & Prochaska, 1998). In tobacco addiction, a specific stage or a figure for readiness does not determine a specific treatment, but as has been stressed above, it has a predictive value about the possible success of the behaviour of change.

Considering the representativeness of the sample studied and its development in the real environment of community care, our study may illustrate the real chances of success of administering the brief anti-tobacco intervention in BD patients and shows that it can be a simple, cost-effective first step which paves the way for more specific interventions which would aim at producing change. In any case, we must be aware of the difficulty of the problem being addressed and controlled studies with larger samples are needed as a first step to confirm the effectiveness of this type of intervention in clinical practice, and as a way to assess objectively the influence of factors such as cognitive performance. We evaluated neurocognitive factors by means of a validated survey, the COBRA questionnaire. Nevertheless, subjective perception of neurocognitive functioning does not always correlate with objective performance on neuropsychological tests and this remains a matter of debate (Miskowiak et al., 2016). Future studies should use formal neuropsychological batteries to confirm or refute the results of this study.

Finally, identifying predictors of motivation/abstinence in further studies of smokers with BD may help devise novel treatments for nicotine addiction. Interventions such as cognitive and functional remediation have proved to be effective in BD (Torrent et al., 2013). Moreover, from a public health perspective, smoking cessation programs aimed at patients with BD could take into account the potential limiting effects of neurocognitive dysfunction to enhance their motivation to quit smoking.

Conflict of interest

V.B.-M. has received grants and served as consultant, advisor or continuing medical education (CME) speaker during the last 5 years for the following entities: Angelini Spain, Angelini Portugal, AstraZeneca, Bristol-Myers-Squibb, Ferrer, Janssen. Juste, Lundbeck, Nutrición Médica, and Otsuka. JA Alcalá-Partera has served as advisor to: Adamed, Lundbeck, Otsuka, Janssen-Cilag, Pfizer, Rovi y Servier; and as speaker to: Janssen-Cilag, Pfizer y Servier. L. Gutiérrez-Rojas has been speaker for and advisory board member of Bristol-Myers Squibb, Janssen-Cilag, Astra-Zeneca, Rovi, Lundbeck, Otsuka, GSK and Pfizer.

All other researchers report no biomedical financial interests or potential conflicts of interests.

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References

- Aharonovich, E., Brooks, A. C., Nunes, E. V. & Hasin, D. S. (2008). Cognitive deficits in marijuana users: Effects on motivational enhancement therapy plus cognitive behavioral therapy treatment outcome. *Drug and Alcohol Dependence*, 95, 279-283. doi:10.1016/j.drugalcdep.2008.01.009.
- Al-Halabí, S., Fernández-Artamendi, S., Díaz-Mesa, E.M., García-Álvarez, L., Flórez, G., Martínez-Santamaría, E.,... Bobes J. (2016). Tobacco and cognitive performance in schizophrenia patients: the design of the COGNICO study. *Adicciones*, 29, 6-12. doi:10.20882/adicciones.724.
- Almadana Pacheco, V., Gómez-Bastero Fernández, A.P., Valido Morales, A., Luque Crespo, E., Monserrat, S. & Montemayor Rubio, T. (2017). Anxiety, depression and tobacco abstinence. *Adicciones*, 29, 233-244. doi:10.20882/adicciones.761.
- Anthenelli, R. M., Benowitz, N. L., West, R., St Aubin, L., McRae, T., Lawrence, D.,... Evins, A.E. (2016). Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. *Lancet*, 387, 2507-2520. doi:10.1016/S0140-6736(16)30272-0.
- Ashare, R.L., Falcone, M. & Lerman, C. (2014). Cognitive function during nicotine withdrawal: Implications for nicotine dependence treatment. *Neuropharmacology*, 76 Pt B, 581-591. doi:10.1016/j.neuropharm.2013.04.034.
- Balanzá-Martínez, V., Crespo-Facorro, B., González-Pinto, A. & Vieta, E. (2015). Bipolar disorder comorbid with alcohol use disorder: focus on neurocognitive correlates. *Frontiers in Physiology*, 6, 108. doi:10.3389/fphys.2015.00108.
- Baune, B.T. & Malhi, G.S. (2015). A review on the impact of cognitive dysfunction on social, occupational, and general functional outcomes in bipolar disorder. *Bipolar Disorders*, 17 (Suppl 2), 41-55. doi:10.1111/bdi.12341.
- Biener, L. & Abrams, D.B. (1991). The Contemplation Ladder: validation of a measure of readiness to consider smoking cessation. *Health Psychology*, 10, 360-365.
- Borland, R., Yong, H.H., Balmford, J., Cooper, J., Cummings, K.M., O'Connor, R.J.,... Fong, G.T. (2010). Motivational factors predict quit attempts but not maintenance of smoking cessation: findings from the International Tobacco Control Four country project. *Nicotine and Tobacco Research*, 12 Suppl, S4-11. doi:10.1093/ntr/ntq050.
- Callaghan, R.C., Veldhuizen, S., Jeysingh, T., Orlan, C., Graham, C., Kakouris, G.,... Gatley, J. (2014). Patterns of tobacco-related mortality among individuals diagnosed with schizophrenia, bipolar disorder, or depression. *Journal of Psychiatry Research*, 48, 102-110. doi:10.1016/j.jpsychires.2013.09.014.
- Cazard, F. & Ferreri, F. (2013). Bipolar disorders and comorbid anxiety: prognostic impact and therapeutic challenges. *Encephale* 39, 66-74. doi:10.1016/j.encep.2012.04.005.
- Ceccarini, M., Borrello, M., Pietrabissa, G., Manzoni, G.M. & Castelnuovo, G. Assessing motivation and readiness to change for weight management and control: an in-depth evaluation of three sets of instruments. *Frontiers in Psychology*, 6, 511. doi:10.3389/fpsyg.2015.00511.
- Chengappa, K.N., Perkins, K.A., Brar, J.S., Schlicht, P.J., Turkin, S.R.,... George, T.P. (2014). Varenicline for smoking cessation in bipolar disorder: a randomized, double-blind, placebo-controlled study. *Journal Clinical of Psychiatry*, 75, 765-772. doi:10.4088/JCP.13m08756.
- Chou, K., Chen, H.K., Hung, C.H., Chen, T.T., Chen, C.M. & Wu, B.J. (2015). Readiness to quit as a predictor for outcomes of smoking-reduction programme with transdermal nicotine patch or bupropion in a sample of 308 patients with schizophrenia. *European Archives of Psychiatry and Clinical Neuroscience*, 265, 249-257. doi:10.1007/s00406-014-0515-7.
- CIE-10., 1992. *Trastornos mentales y del comportamiento, descripciones clínicas y pautas para el diagnóstico*. Madrid: Meditor.
- de Leon, J., Diaz, F.J., Aguilar, M.C., Jurado, D. & Gurpegi, M. (2006). Does smoking reduce akathisia? Testing a narrow version of the self-medication hypothesis. *Schizophrenia Research*, 86, 256-268. doi:10.1016/j.schres.2006.05.009.
- Diaz, F.J., James, D., Botts, S., Maw, L., Susce, M.T. & de Leon, J. (2009). Tobacco smoking behaviors in bipolar disorder: a comparison of the general population, schizophrenia, and major depression. *Bipolar Disorders*, 11, 154-165. doi:10.1111/j.1399-5618.2009.00664.x.
- DiClemente, C.C., Prochaska, J.O., Fairhurst, S.K., Velicer, W.F., Velasquez M.M. & Rossi, J.S. (1991). The process of smoking cessation: An analysis of precontemplation, contemplation, and preparation stages of change. *Journal of Consulting and Clinical Psychology*, 59, 295-304.

- DiClemente, C.C. & Prochaska, J.O. (1998). *Toward a comprehensive, transtheoretical model of change: stages of change and addictive behavior*. In: Miller WR, Heather N, eds. *Treating Addictive Behaviors*. 2nd ed. New York, Plenum. Pp: 3-24.
- DiClemente, C.C., Schlundt, D. & Gemmell, L. (2004). Readiness and stages of change in addiction treatment. *American Journal on Addictions*, 13, 103-119. doi:10.1080/10550490490435777.
- DiClemente, C.C., Delahanty, J.C., Kofeldt, M.G., Dixon, L., Goldberg, R. & Lucksted, A. (2011). Stage movement following a 5A's intervention in tobacco dependent individuals with serious mental illness (SMI). *Addictive Behaviour*, 36, 261-264. doi:10.1016/j.addbeh.2010.11.002.
- Etter, M. & Etter, J.F. (2004). Alcohol consumption and the CAGE test in outpatients with schizophrenia or schizoaffective disorder and in the general population. *Schizophrenia Bulletin*, 30, 947-956.
- Evins, A.E., Cather, C. & Laffer, A. (2015). Treatment of tobacco use disorders in smokers with serious mental illness; toward clinical best practices. *Harvard Review of Psychiatry*, 23, 90-98. doi:10.1097/HRP.0000000000000063.
- Fagerström, K.O. (1978). Measuring degree of physical dependence to tobacco smoking with reference to individualization of treatment. *Addictive Behaviour*, 3, 235-241.
- Fiore, M. & Panel, G. (2008). *Treating tobacco use and dependence: 2008 update*. Rockville MD: Department of Health and Human Services.
- García-Portilla, M.P., Saiz, P.A., Benabarre, A., Florez, G., Bascaran, M.T., Díaz, E.M.,... Bobes, J. (2010). Impact of substance use on the physical health of patients with bipolar disorder. *Acta Psychiatrica Scandinavica*, 121, 437-445. doi:10.1111/j.1600-0447.2009.01498.x.
- García-Portilla, M.P., García-Álvarez, L., Sarraimea, F., Galvan, G., Díaz-Mesa, E., Bobes-Bascaran, T.,... Bobes, J. (2016). It is feasible and effective to help patients with severe mental disorders to quit smoking: an ecological pragmatic clinical trial with transdermal nicotine patches and varenicline. *Schizophrenia Research*, 176, 272-280. doi:10.1016/j.schres.2016.05.011.
- George, T.P., Wu, B.S. & Weinberger, A.H. (2012). A review of smoking cessation in bipolar disorder: implications for future research. *Journal of Dual Diagnosis*, 8, 126-130. doi:10.1080/15504263.2012.671717.
- Goes, F.S. (2015). The importance of anxiety states in bipolar disorder. *Current Psychiatry Reports*, 17, 3. doi:10.1007/s11920-014-0540-2.
- Gómez-Peña, M., Penelo, E., Granero, R., Fernández-Aranda, F., Álvarez-Moya, E., Santamaría, J.J.,... Jiménez-Murcia, S. (2011). Motivation to change and pathological gambling: analysis of the relationship with clinical and psychopathological variables. *British Journal of Clinical Psychology*, 50, 196-210. doi:10.1348/014466510X511006.
- Gonzalez-Pinto, A., Gutierrez, M., Ezcurra, J., Aizpuru, F., Mosquera, F., López, P. & de Leon, J. (1998). Tobacco smoking and bipolar disorder. *Journal of Clinical Psychiatry*, 59, 225-228.
- Gutiérrez-Rojas, L., Gurpegui, M., Ayuso-Mateos, J.L., Gutiérrez-Ariza, J.A., Ruiz-Veguilla, M. & Jurado, D. (2008). Quality of life in bipolar disorder patients: a comparison with a general population sample. *Bipolar Disorders*, 10, 625-634. doi:10.1111/j.1399-5618.2008.00604.x.
- Gwaltney, C.J., Metrik, J., Kahler, C.W. & Shiffman, S. (2009). Self-efficacy and smoking cessation: a meta-analysis. *Psychol. Addictive Behaviour*, 23, 56-66. doi:10.1037/a0013529.
- Hamilton, M. (1959). The assessment of anxiety states by rating. *British Journal of Medical Psychology*, 32, 50-55.
- Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry*, 23, 56-62.
- Heatherton, T.F., Kozlowski, L.T., Frejcek, R.C. & Fagerström, K.O. (1991). The Fagerström Test for Nicotine Dependence: A revision of the Fagerström Tolerance Questionnaire. *British Journal of Addiction*, 86, 1119-1127.
- Heffner, J.L., Strawn, J.R., DelBello, M.P., Strakowski, S.M. & Anthenelli, R.M. (2011). The co-occurrence of cigarette smoking and bipolar disorder: phenomenology and treatment considerations. *Bipolar Disorders*, 13, 439-453. doi:10.1111/j.1399-5618.2011.00943.x.
- Jackson, J.G., Diaz, F.J., Lopez, L., de Leon, J. (2015). A combined analysis of worldwide studies demonstrates an association between bipolar disorder and tobacco smoking behaviors in adults. *Bipolar Disorders*, 17, 575-597. doi:10.1111/bdi.12319.
- Japuntich, S.J., Leventhal, A.M., Piper, M.E., Bolt, D.M., Roberts, L.J., Fiore, M.C. & Baker, T.B. (2011). Smoker characteristics and smoking-cessation milestones. *American Journal of Preventive Medicine*, 40, 286-294. doi:10.1016/j.amepre.2010.11.016.
- Kruger, J., O'Halloran, A., Rosenthal, A.C., Babb, S.D. & Fiore, M.C. (2016). Receipt of evidence-based brief cessation interventions by health professionals and use of cessation assisted treatments among current adult cigarette-only smokers: National Adult Tobacco Survey, 2009-2010. *BMC Public Health*, 16, 141. doi:10.1186/s12889-016-2798-2.
- Marín Romero, B., Gil Roales-Nieto, J. & Moreno San Pedro, E. (2017). Self-quit in a Spanish sample. An exploratory study. *Adicciones*, 29, 210-212. doi:10.20882/adicciones.925.
- Miller, W.R. (2011). *Motivational factors in addictive behaviors*. In: Miller WR and Carroll KM, (Eds). *Rethinking substance abuse: What the science shows and what we should do about it*. New York: Guilford Press, pp. 134-152.
- Miskowiak, K.W., Petersen, J.Z., Ott, C.V., Knorr, U., Kessing, L.V., Gallagher, P. & Robinson, L. (2016). Predictors of the discrepancy between objective and subjective

- cognition in bipolar disorder: a novel methodology. *Acta Psychiatrica Scandinavica*, 134, 511-521.
- Moss, T.G., Sacco, K.A., Allen, T.M., Weinberger, A.H., Vesicchio, J.C. & George, T.P. (2009). Prefrontal cognitive dysfunction is associated with tobacco dependence treatment failure in smokers with schizophrenia. *Drug and Alcohol Dependence*, 104, 94-99. doi:10.1111/acps.12649.
- Prochaska, J.O. & DiClemente, C.C. (1983). Stages and processes of self-change of smoking: toward an integrative model of change. *Journal of Consulting and Clinical Psychology*, 51, 390-395.
- Prochaska, J.J., Reyes, R.S., Schroeder, S.A., Daniels, A.S., Doederlein, A. & Bergeson, B. (2011). An online survey of tobacco use, intentions to quit, and cessation strategies among people living with bipolar disorder. *Bipolar Disorders*, 13, 466-473. doi:10.1111/j.1399-5618.2011.00944.x.
- Rhodes, J.D. & Hawk, L.W. JR. (2016). Smoke and mirrors: The overnight abstinence paradigm as an index of disrupted cognitive function. *Psychopharmacology*, (Berl). 233, 1395-1404. doi:10.1007/s00213-016-4227-8.
- Rice, V.H. & Stead, L.F. (2008). Nursing interventions for smoking cessation. *Cochrane Database Systematic Review*, CD001188. doi:10.1002/14651858.CD001188.pub3.
- Rosa, A.R., Mercadé, C., Sánchez-Moreno, J., Solé, B., Mar Bonnin, C.D., Torrent, C.,... Martínez-Arán, A. (2013). Validity and reliability of a rating scale on subjective cognitive deficits in bipolar disorder (COBRA). *Journal of Affective Disorders*, 150, 29-36. doi:10.1016/j.jad.2013.02.022.
- Rüther, T., Bobes, J., De Hert, M., Svensson, T.H., Mann, K., Batra, A.,... Möller, H.J. (2014). EPA guidance on tobacco dependence and strategies for smoking cessation in people with mental illness. *European Psychiatry*, 29, 65-82. doi:10.1016/j.eurpsy.2013.11.002.
- Schroeder, S.A. (2014). Even more illness caused by smoking than previously estimated. *JAMA Internal Medicine*, 174, 1928-1929. doi:10.1001/jamainternmed.2014.4297.
- Sharma, A. & Szatkowski, L. (2014). Characteristics of smokers who have never tried to quit: evidence from the British Opinions and Lifestyle Survey. *BMC Public Health*, 14, 346. doi:10.1186/1471-2458-14-346.
- Siru, R., Hulse, G.K. & Tait, R.J. (2009). Assessing motivation to quit smoking in people with mental illness: a review. *Addiction*, 104, 719-733. doi:10.1111/j.1360-0443.2009.02545.x.
- Tidey, J.W. & Miller, M.E. (2015). Smoking cessation and reduction in people with chronic mental illness. *BMJ*, 351, h4065. doi:10.1136/bmj.h4065.
- Torrent, C., Bonnin, C del M., Martínez-Arán, A., Valle, J., Amann, B.L., González-Pinto, A.,... Vieta, E. (2013). Efficacy of functional remediation in bipolar disorder: a multicenter randomized controlled study. *American Journal of Psychiatry*, 170, 852-859. doi:10.1176/appi.ajp.2012.12070971.
- Vieta, E., Popovic, D., Rosa, A.R., Solé, B., Grande, I., Frey, B.N.,... Kapczinski, F. (2013). The clinical implications of cognitive impairment and allostatic load in bipolar disorder. *European Psychiatry*, 28, 21-29. doi:10.1016/j.eurpsy.2011.11.007.
- Weinberger, A.H., Krishnan-Sarin, S., Mazure, C.M. & McKee, S.A. (2008). Relationship of perceived risks of smoking cessation to symptoms of withdrawal, craving, and depression during short-term smoking abstinence. *Addictive Behaviour*, 33, 960-963. doi:10.1016/j.addbeh.2008.02.013.
- West, R., McNeill, A. & Raw, M. (2000). Smoking cessation guidelines for health professionals: an update. Health Education Authority. *Thorax*, 55, 987-999. doi:10.1016/j.eurpsy.2011.11.007.
- West, R., Raw, M., McNeill, A., Stead, L., Aveyard, P., Bitton, J.,... Borland, R. (2015). Health-care interventions to promote and assist tobacco cessation: a review of efficacy, effectiveness and affordability for use in national guideline development. *Addiction*, 110, 1388-1403. doi:10.1111/add.12998.
- Wu, B.S., Weinberger, A.H., Mancuso, E., Wing, V.C., Haggi-Khamneh, B., Levinson, A.J. & George, T.P. (2012). A Preliminary Feasibility Study of Varenicline for Smoking Cessation in Bipolar Disorder. *Journal of Dual Diagnosis*, 8, 131-132. doi:10.1080/15504263.2012.671067.
- Young, R.C., Biggs, J.T., Ziegler, V.E. & Meyer, D.A. (1978). A rating scale for mania: reliability, validity and sensitivity. *British Journal of Psychiatry*, 133, 429-435.
- Zolnieriek, K.B. & Dimatteo, M.R. (2009). Physician communication and patient adherence to treatment: a meta-analysis. *Medical Care*, 47, 826-834. doi:10.1097/MLR.0b013e31819a5acc.

